Clinical Trial Report Summary – Study 10067

Title of Study
An open, multicentre, prospective, randomised study assessing the impact of educational information on treatment outcome in depressed outpatients treated with escitalopram

Study Centres
30 centres in Finland

Study Period
First patient first visit – 16 June 2003
Last patient last visit – 17 June 2004

Objectives
The objectives were:
• to assess - in depressed outpatients treated with escitalopram for 16 weeks - the impact of educational information on:
  – Montgomery-Åsberg Depression Rating Scale (MADRS)
  – Clinical Global Impression – Global Improvement (CGI-I)
  – Patient Global Evaluation (PGE)
• to evaluate with Hopkins Symptom Checklist (SCL-90) the symptom profile and treatment response in depression
• to obtain information about treatment outcome and tolerability of escitalopram in the treatment of a broad population of depressed outpatients

Methodology
• Open-label, multicentre, prospective, single-blind study for assessing impact of educational information.
• Patients who gave written informed consent at the baseline visit underwent screening assessments. If all inclusion criteria and none of the exclusion criteria were fulfilled, the patients were included in the study.
• Patients received escitalopram treatment according to the Summary of Product Characteristics (SPC) for 16 weeks. Patients were randomised to receive educational information in addition to treatment or not. Patients received the information letters during weeks 1, 4, 10.

Number of Patients Planned and Analysed
• Approximately 180 patients were planned for the study.
• A total of 79 patients received escitalopram with educational information, while 78 patients received escitalopram without educational information.
• Patient disposition is tabulated below:

<table>
<thead>
<tr>
<th>Escitalopram 10-20 mg</th>
<th>n</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients enrolled 158</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients treated (APTS): 157</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients completed 132 (84.1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients withdrawn 25 (15.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary reason for withdrawal:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adverse events (AEs) 11 (7.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lack of efficacy 1 (0.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Analysis set: Full-analysis set (FAS) 150</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

n = number of patients; % = percentage of patients enrolled
Diagnosis and Main Selection Criteria

Patients who:
- gave their signed informed consent
- suffered from acute episode of depression requiring pharmacological treatment according to the SPC for escitalopram
- were ≥18 years of age

Investigational Product, Dose and Mode of Administration

Escitalopram – 10 or 20mg once daily; orally

Duration of Treatment

16 weeks

Criteria for Evaluation – Efficacy

- **Primary variable** – change from baseline in MADRS total score
- **Secondary variables:**
  - CGI-I
  - PGE
  - SCL-90

Criteria for Evaluation – Safety

AEs

Statistical Methods

- The following analysis sets were used:
  - *all-patients-treated set* (APTS) – all patients who took at least one dose of study medication
  - *full-analysis set* (FAS) – all patients who took at least one dose of study medication and who had at least one valid post-baseline assessment of the primary efficacy variable
- All efficacy analyses were conducted for the FAS. All safety analyses were conducted for the APTS.
- The primary efficacy analysis - the change in the MADRS total score from baseline to end of treatment was analysed using analysis of covariance (ANCOVA) with baseline score as covariate and with treatment group and centre as factors.
- Last observation carried forward (LOCF) was used for missing values. The influence of covariates was studied by including terms in the primary ANCOVA model, either as main effects or as main effects together with terms for interaction with treatment.
- The secondary efficacy analyses - the change from baseline in MADRS total score using the observed cases (OC) approach at Week 6 and Week 16.
- The change in CGI-I, PGE and SCL-90 scores was analysed using the same methods.
- Response rates (≥50% decrease in MADRS total score from baseline)
- Change from baseline in SCL-90 total score as well as anxiety, depression, somatic subscores and sleep items (44, 64, and 66) was analysed as above (both LOCF and OC).
- The primary safety parameter was the number and frequency of AEs over the 16-week treatment period in the whole population.

Demography of Study Population

- The mean age was 44 ± 10 years (range 18 to 62) and the majority of patients were women (76%).
- The mean baseline severity of depressive symptoms measured with MADRS total score was 25.3.
Efficacy Results

- There was a continuous improvement in depressive symptoms throughout the 16-week treatment period as assessed by MADRS total score. Results were similar when analysed using LOCF and OC methods.
- The mean MADRS total score decreased from 25.3 at baseline to 7.9 at Week 16 (LOCF).
- At study end, response rates were 81.6% in educational and 78.4% in non-educational group (non-significant).
- CGI-I and PGE showed the same level of improvement. There was a statistically significant (p<0.001) correlation between these two scales indicating a consistent evaluation of the improvement of depressive symptoms by both patients and investigators.
- Patient symptoms seemed to improve slightly more in the non-educational group (change - 69.1 and - 78.1) (non-significant).
- For the somatisation subscore of the SCL-90 the difference was significantly (p=0.04) in favour of the non-educational group.
- On the sleep items (44, 64, and 66) of the SCL-90 patients in the non-educational group tended to show better improvement (p=0.08).

Safety Results

- The AE incidence is summarised below:

<table>
<thead>
<tr>
<th>Escitalopram 10-20 mg</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients who died</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Patients with SAEs</td>
<td>5 (3%)</td>
</tr>
<tr>
<td>Patients with AEs</td>
<td>113 (72%)</td>
</tr>
</tbody>
</table>

n = number of patients; % = percentage of patients enrolled

- AEs with an incidence ≥5% are summarised below:

<table>
<thead>
<tr>
<th></th>
<th>Educational information received</th>
<th>No educational information received</th>
<th>Total n=157</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>19 (24.1%)</td>
<td>20 (25.6%)</td>
<td>39 (24.8%)</td>
</tr>
<tr>
<td>Headache</td>
<td>14 (17.7%)</td>
<td>10 (12.8%)</td>
<td>24 (15.3%)</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>11 (13.9%)</td>
<td>10 (12.8%)</td>
<td>21 (13.4%)</td>
</tr>
<tr>
<td>Sweating increased</td>
<td>7 (8.9%)</td>
<td>12 (15.4%)</td>
<td>19 (12.1%)</td>
</tr>
<tr>
<td>Dizziness</td>
<td>4 (5.1%)</td>
<td>12 (15.4%)</td>
<td>16 (10.2%)</td>
</tr>
<tr>
<td>Insomnia</td>
<td>6 (7.6%)</td>
<td>7 (9.0%)</td>
<td>13 (8.3%)</td>
</tr>
<tr>
<td>Anorexia</td>
<td>4 (5.1%)</td>
<td>6 (7.7%)</td>
<td>10 (6.4%)</td>
</tr>
<tr>
<td>Mouth dry</td>
<td>4 (5.1%)</td>
<td>4 (5.1%)</td>
<td>8 (5.1%)</td>
</tr>
</tbody>
</table>

n = number of patients

- The majority of AEs were mild in severity, while 13 patients reported severe AEs. AEs experienced in 71 patients (45%) were considered probably related to study medication.
- There was no difference in the safety profile between the two groups.

Publications


This study was conducted in compliance with the principles of *Good Clinical Practice*. 